DAVID CHIU, State Bar # 189542
City Attorney
YVONNE R. MERE, State Bar # 175394
Chief Deputy City Attorney
SARA J. EISENBERG, State Bar # 296303
Chief of Complex & Affirmative Litigation
OWEN J. CLEMENTS, State Bar # 141805
JAIME M. HULING DELAYE, State Bar # 270784
JOHN H. GEORGE, State Bar # 292332
Deputy City Attorneys
Fox Plaza
1390 Market Street, Sixth Floor
San Francisco, CA 94102
Telephone: 415.554.3597
jaime.hulingdelaye@sfcityatty.org

Attorneys for Plaintiff The People of the State of California, acting by and through San Francisco City Attorney David Chiu

[Additional counsel appear on signature page.]

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN FRANCISCO DIVISION

THE CITY AND COUNTY OF SAN FRANCISCO, CALIFORNIA and THE PEOPLE OF THE STATE OF CALIFORNIA, Acting by and through San Francisco City Attorney DAVID CHIU,

Plaintiff,

v.

PURDUE PHARMA L.P., et al.

Defendants.

Case No. 3:18-cv-07591-CRB

SUMMARY OF DECLARATION OF ANNA LEMBKE, M.D.

Judge: Honorable Charles R. Breyer

I. Background and Qualification

I am Professor, Chief of the Addiction Medicine Dual Diagnosis Clinic, Medical Director of Addiction Medicine, and Program Director of the Addiction Medicine Fellowship, in the Department of Psychiatry and Behavioral Sciences at Stanford University School of Medicine. From 2016 to 2021 I also held a Courtesy Appointment in the Stanford University Department of Anesthesiology and Pain Medicine. I began my faculty career at Stanford in 2003. I was first retained in opioid litigation in January 2018, by the attorneys representing plaintiffs in the Opioid Multidistrict Litigation. Since that time, I have testified at three trials, five depositions, and two hearings regarding admissibility of expert testimony. My rate of compensation is $500 per hour, or $800 per hour for testimony at deposition or trial.

In forming the opinions that follow, I have relied on my medical training, more than twenty years of clinical experience treating addiction and pain, and my own research on opioid prescribing. My research began circa 2001 and has been multimodal. I have done qualitative interviews with patients, providers, and others in the health care field on questions related to opioid prescribing. I have followed and analyzed the medical literature using PubMed and other academic search engines, along with different combinations of key words such as "pain, opioids, treatment, randomized clinical trials, open label trials, effectiveness, adverse effects, prescribing, addiction, dependence, overdose, etc. …" I have compiled statistics published by the CDC and other government agencies. I have, in collaboration with colleagues, analyzed opioid prescribing databases such as Medicare Part D. As a regular and ongoing part of my practice, I conduct literature searches of research on the subjects of addiction and pain treatment, which is essential to my work with my patients. Indeed, given the large and increasing role of opioid drugs in addiction, the fields of addiction and pain medicine are inevitably intertwined, such that it is essential to my practice to remain aware of the state of scientific inquiry in both fields. I hold the opinions stated here to a reasonable degree of scientific certainty:

A. Opinion 1

Addiction is a chronic, relapsing and remitting disease with a behavioral component, characterized by neuroadaptive brain changes resulting from exposure to addictive drugs. Every human being has the potential to become addicted. Some are more vulnerable than others. Risks for becoming addicted include genetic, developmental, and environmental factors (nature, nurture, and neighborhood). One of the biggest risk factors for addiction is simple access to addictive drugs. When supply of an addictive drug is increased, more people become addicted to and suffer the harms of that drug. Prescription opioids are as addictive as heroin.

B. Opinion 2

The addictive nature of medicinal opioids has been known for centuries. Misrepresentations of the safety and efficacy of prescription opioids, by Teva, Allergan and their affiliates, as well as by Walgreens through mis-education of their pharmacists, reversed a century of appropriate restrictions on the use of these dangerous drugs, and substantially contributed to the current opioid epidemic.

C. Opinion 3

Opioid prescribing began to increase in the 1980s and became prolific in the 1990s and the early part of the 21st century, representing a radical paradigm shift in the treatment of pain and creating more access to opioids across the United States, which in turn increased the risk of opioid addiction and overdose death.

D. Opinion 4

Teva, Allergan and Walgreens contributed substantially to the paradigm shift in opioid prescribing through misleading messaging about the safety and efficacy of prescription opioids.

I have reviewed promotional materials that included false and misleading statements made or promoted by the Defendants in this case. These misleading statements fall into at least seven different categories of misrepresentations, each of which is refuted by the best science available:

Categories of Defendants' Misrepresentations	Refutation by the Best Science Available
(1) *Addiction to prescription opioids is rare or virtually nonexistent in patients treated for chronic pain under a doctor's care, and only "addicts" are at risk of addiction to prescription opioids.* • Allergan: "addiction is quite rare." • Teva: "3.27%...likelihood of abuse/addiction" • Walgreens: "exquisitely rare."	(1) Contrary to Defendants' misrepresentations that the risk of addiction to prescription opioids is "rare," or "less than 1%", there was ample evidence available to Defendants before and during their promotional campaigns, that in fact prescription opioids are as addictive as heroin, and the risk of addiction is far higher than stated by the Industry. The best data show an opioid addiction prevalence of at least 10-30% among chronic pain patients prescribed opioids including the range of mild, moderate, and severe addiction/opioid use disorder (OUD).
(2) *There is no clinical "ceiling dose" of prescription opioids, in contrast to other pain relief medications, so opioids can be uptitrated without concern of harm.* • Allergan: "no absolute ceiling effect" • Teva: "There is no ceiling dose as there is with the NSAIDs."	(2) Contrary to Defendants' misleading representations of "no ceiling dose", the risk of overdose and death increases dramatically as the dose and duration of opioid exposure are increased; and the false comparison of NSAIDs to opioids overstates the numbers of deaths with NSAIDs and does not disclose that opioids have a higher mortality rate than NSAIDs.
(3) *Drug-seeking behavior in patients receiving opioid therapy is not a sign of addiction but rather pseudoaddiction, and these patients are experiencing under-treated*	(3) Contrary to Defendants' claims, there is no empirical support for the diagnosis of *pseudoaddiction*.

Categories of Defendants' Misrepresentations	Refutation by the Best Science Available
pain requiring more opioids. • Allergan: "Pseudoaddiction is drug-seeking behavior that seems similar to addiction" • Teva: "If patients receive inadequate pain relief, they may exhibit drug-seeking behaviors. This is called pseudoaddiction." • Walgreens: "Pseudoaddiction can be differentiated from drug misuse by increasing the dose…"	
(4) *Opioids are effective, first-line treatment for chronic pain.* • Allergan: "Why don't you use Kadian first line?" • Teva: "Despite the great benefits of opioids, they are often under-used." • Teva/Cephalon: "It is a myth that opioids, like morphine should only be used at the final stages of a seriously painful disease."	(4) There is no reliable scientific evidence that long-term opioid therapy is effective for chronic non-cancer pain. Evidence of short-term benefit (12 weeks or less) in people with chronic pain is not evidence of efficacy for long-term use. There is robust evidence that long-term opioid therapy leads to severe harms. As such, anecdotal reports of long-term benefit are not sufficient to outweigh the overwhelming evidence of long-term harms to the individual and the public health. Opioids are the least safe intervention when used long-term for chronic pain and should never be "first-line" treatment. The Industry claimed that the failure to prescribe opioids led to the "undertreatment of pain." While there are legitimate concerns about untreated pain in this country, opioids used long-term to treat pain were never the answer, due to the absence of evidence of long-term benefit, and the strong evidence of unacceptable risk. On this subject, I agree with the conclusion in the National Academy of Science, Engineering, and Medicine (NASEM) Report: "The very real problems of underdiagnosis and undertreatment of pain are valid concerns, but it would be a mistake to infer that greater utilization of opioids would ameliorate these problems." This conclusion follows directly from NASEM's conclusion that evidence does not support efficacy of long-term opioids for chronic pain, while the

Categories of Defendants' Misrepresentations	Refutation by the Best Science Available
	risks of such therapy are significant and well-established.
(5) *Dependence is a benign and easily treated condition, dependence on opioids is no different from dependence on other drugs, like blood-pressure medications, and breakthrough pain is not a sign of decreasing efficacy, but a sign of needing more potent and faster acting opioids on top of longer-acting opioids.* • Allergan: "Physical dependence simply requires a tapered withdrawal should the opioid medication no longer be needed." • Teva: "Physical dependence is normal"	(5) Contrary to Defendants' misrepresentations, opioid dependence is debilitating for many and opioid tapering is impossible for some. Prescription opioids induce physiological dependence almost universally, and dependence leads to addiction in a significant subset of users, particularly as dose and duration of exposure are increased. Breakthrough pain in the context of chronic pain inappropriately normalizes escalating doses and encourages routine use of highly potent and lethal opioids like fentanyl. The concept of breakthrough pain was particularly harmful as used by Teva to promote Actiq and Fentora (fentanyl). While Actiq and Fentora were approved only for breakthrough cancer pain, they were widely promoted and sold for non-cancer pain (over 90% of prescriptions were for non-cancer pain), thereby exposing many more people to their risks.
(6) *"Screening tools" can identify who will become addicted.* • Teva: "In terms of screening, there are various instruments that we can use as healthcare providers to identify the risk of opioid abuse in our patients…"	(6) Although it is true that people with a history of addiction and/or mental illness are at higher risk of addiction to prescription opioids, it is also true that there are no reliable screening tools to prospectively predict who will become addicted to prescription opioids. Further, persons without pre-existing risk factors can also become addicted, and the biggest predictor of addiction is opioid dose and duration, rather than individual patient characteristics.
(7) *Abuse Deterrent Formulations decrease risk and addiction.* • Teva: "The pharmaceutical industry has also stepped up and is trying to play a role in preventing the misuse and…through the development of abuse-deterrent formulations for opioids."	(7) This is misleading because the focus on unproven abuse-deterrent formulations detracts from the fact that the most common way that people misuse and get addicted to prescription opioids is through ingesting oral formulations as prescribed.

E. Opinion 5

Teva and Allergan disseminated these misleading messages through an aggressive sales force, key opinion leaders, medical school curricula, continuing medical education courses, seeding the medical literature, clinical decision support tools, professional medical societies, patient advocacy groups, the Federation of State Medical Boards, state legislation, and The Joint Commission.

F. Opinion 6

Walgreens leveraged its unique and pivotal position in the opioid supply chain to contribute to the unprecedented and unchecked flow of opioid pain pills into the community. Walgreens had direct contact with opioid manufacturers and distributors upstream, and patients and prescribers downstream. Walgreens' efforts to "create demand" included building opioid "Super Stores" to enhance unrestricted flow of opioid pain pills, spreading misinformation about the safety and efficacy of opioid pain pills, partnering with pro-opioid industry advocacy and lobbying organizations, ignoring "red flags" for misuse and diversion including concerns expressed by their own pharmacists, and failing to use or analyze their own dispensing data to assist pharmacists in identifying red flags. By increasing and assuring the supply of opioids and failing to provide effective controls against diversion, Walgreens contributed to opioid misuse, addiction, dependence, and death.

G. Opinion 7

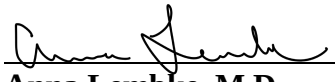
The increased supply of prescription opioids through licit and illicit sources, and the natural progression from prescription opioids to heroin and illicit fentanyl, resulted in an opioid epidemic in the United States. "Epidemic," defined as an outbreak of disease that spreads quickly and affects many individuals at the same time, is the appropriate term to describe the increase in opioid related morbidity and mortality beginning in the 1990's and continuing to the present day.

II. Conclusion

Addiction is a chronic, relapsing and remitting disease with a behavioral component, characterized by neuroadaptive brain changes resulting from exposure to addictive drugs. One of the biggest risk factors for addiction is simple access to addictive drugs. When supply of an addictive drug is increased, more people become addicted to and suffer the harms of that drug. The Defendants' conduct in promoting increased supply and widespread access to prescription opioids, including through misleading messaging and unchecked distribution and dispensing, has resulted in an epidemic of opioid addiction and overdose death. Others bear some lesser responsibility for the opioid epidemic. However, today's opioid crisis would not have occurred without the paradigm shift substantially caused by Defendants and others in the pharmaceutical opioid industry.

Pursuant to 28 U.S.C. S 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed on: April 24, 2022



Anna Lembke, M.D.